1636

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/846,588
Filing Date	May 1, 2001
First Named Inventor	Goldman et al.
Group Art Unit	1636
Examiner Name	Q. Nguyen
Total Number of Pages in This Submission	
Attorney Docket Number	19603/3232 (CRF D-2587B)

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☒ Supplemental Response/Reply ($_____)
  - ☐ After Final
  - ☒ Affidavits/declaration(s)
- ☐ Extension of Time Request ($_____)
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement ($____)
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Notice to File Missing Parts/ Incomplete Application ($_____)
  - ☐ A copy of the Notice to File Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Assignment Papers *(for an Application)*
- ☐ Drawing(s)
- ☐ Declaration and Power of Attorney
- ☐ Licensing-related Papers
- ☐ Petition ($_____)
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer ($_____)
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group ($____) (Appeal Notice, Brief, Reply Brief)
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Application Data Sheet
- ☐ Request for Corrected Filing Receipt with Enclosures
- ☒ A self-addressed, prepaid postcard for acknowledging receipt
- ☐ Other Enclosure(s) *(please identify below)*:
- ☐ Check in the amount of $_____

Remarks

☒ The Commissioner is hereby authorized to charge any additional fees required or credit any overpayments to Deposit Account No. 14-1138 for the above identified docket number.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm *or* Individual name	Michael L. Goldman Nixon Peabody LLP Clinton Square, P.O. Box 31051 Rochester, New York 14603-1051 Telephone: (585) 263-1304 Fax: (585) 263-1600
Signature	Michael L. Goldman — Registration No. 30,727
Date	December 23, 2004

CERTIFICATE OF MAILING OR TRANSMISSION [37 CFR 1.8(a)]

I hereby certify that this correspondence is being:

☒ deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450

☐ transmitted by facsimile on the date shown below to the United States Patent and Trademark Office at (703) _____.

12/23/04
Date

Wendy L. Barry
Signature

Wendy L. Barry
Typed or printed name

PATENT
Docket No. **19603/3232 (CRF D-2587B)**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Goldman et al.	Examiner: Q. Nguyen
Serial No.	:	09/846,588	
Cnfrm. No.	:	4784	Art Unit: 1636
Filed	:	May 1, 2001	
For	:	METHOD OF INDUCING NEURONAL PRODUCTION IN THE BRAIN AND SPINAL CORD	

SUPPLEMENTAL RESPONSE

MAIL STOP: Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This is further to the Amendment filed on December 2, 2004, regarding the above-identified application. In that response, the rejection of claims 28-30, 33-38, 44-46, and 49 under 35 U.S.C. § 112 (first paragraph) for lack of enablement was traversed.

In further support of that traversal, applicants hereby submit the Declaration of M. Flint Beal, M.D. Under 37 C.F.R. § 1.132 ("Beal Declaration") to explain the significance of the present invention (*Id.* at ¶ 5).

Dr. Beal is an expert in the area of neurodegenerative diseases and their treatment, including Huntington's Disease (Beal Declaration ¶ 4). In particular, his areas of research have included the discovery and evaluation of new pharmacological treatment approaches for Huntington's Disease as well as for related neurodegenerative diseases, including amyotrophic lateral sclerosis (*Id.*). With these credentials, he is fully able to review the data concerning the present invention and discuss its significance.

In making his analysis, Dr. Beal considered the previously submitted Declaration of Steven A. Goldman under 37 C.F.R. § 1.132, the Second Declaration of Steven A. Goldman under 37 C.F.R. § 1.132, and the Third Declaration of Steven A. Goldman Under 37 C.F.R. § 1.132 (Beal Declaration ¶ 5).

Based on this review, Dr. Beal noted that applicants found that viral overexpression of brain-derived neurotrophic factor ("BDNF") in the normal adult rodent

ventricular system induces the generation of new neurons from the neural stem cell population of the ventricular subependyma (Beal Declaration ¶ 6). The new neurons migrate to the olfactory bulb primarily, but a large cohort invades the striatum as well, where they integrate as new striatal neurons (*Id.*). These cells adopt a DARPP32/GABAergic/calbindin+ phenotype, characteristic of the medium spiny neuronal population of the caudate-putamen (*Id.*). This is the predominant neostriatal phenotype lost in Huntington's Disease; as such, applicants postulated that the induced generation of this cell type might be a feasible strategy for slowing or reversing disease progression (*Id.*). In an effort to increase the numbers of neurons generated through this approach, applicants found that the numbers of new neurons recruited to the striatum in response to BDNF were increased by concurrently suppressing subependymal gliogenesis, using adenoviral overexpression of noggin protein (*Id.*). Used together, BDNF and noggin over-expression induced the addition of over 350 new neurons/mm^3/month to the adult rodent neostriatum (*Id.*). This effect is pronounced in both normal mice and rats, and in mouse transgenic models of Huntington's Disease (*Id.*). The new neurons largely assume medium spiny neuronal phenotype, and project to the globus pallidus (*Id.*). These cells are generated in sufficiently high numbers, over a long enough period of time, and with sufficiently robust maturation, survival, and network integration, that they were able to improve deficient striatal function in the R6-2 mouse model of Huntington's Disease ("HD") (*Id.*). Applicants found that when co-injected with both AdBDNF and AdNoggin intraventricularly, the HD mutant mice exhibited a significant delay in disease progression, sustained motor performance, and prolonged survival relative to untreated and null-virus treated controls (*Id.*). In broad terms, these findings indicate that induced neurogenesis may be viewed as a potential therapeutic modality for HD (*Id.*). Specifically, BDNF overexpression is necessary and sufficient to permit the generation in the adult brain of new striatal neurons of the identical phenotype lost in HD (*Id.*). Furthermore, the addition of noggin augments the numbers of these BDNF-induced neurons, so as to provide a feasible and effective treatment approach to HD (*Id.*). As such, these experiments lay both a conceptual and operational foundation for the BDNF and BDNF/noggin-mediated induction of striatal neurogenesis as a therapeutic strategy in HD (*Id.*).

In view of the Beal Declaration and for the reasons set forth in the December 2, 2004, Amendment, applicants hereby respectfully submit that the lack of enablement rejection is improper and should be withdrawn.

Respectfully submitted,

Date: December 23, 2004

Michael L. Goldman
Registration No. 30,727

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603-1051
Telephone: (585) 263-1304
Facsimile: (585) 263-1600

CERTIFICATE OF MAILING OR TRANSMISSION [37 CFR 1.8(a)]

I hereby certify that this correspondence is being:

☒ deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450

☐ transmitted by facsimile on the date shown below to the United States Patent and Trademark Office at (703) _____.

12/23/04
Date

Signature

Wendy L. Barry
Type or Print Name